Data Sheet

Ferrosig

Iron polymaltose 50 mg/ml

Presentation

A slightly viscous, dark reddish brown liquid. Odour faintly malt-like. Each ampoule of FERROSIG contains the equivalent of 100mg of iron.

Uses

Actions

FERROSIG is complexed in an aqueous, approximately isotonic solution for intramuscular injection. The complex is stable over a wide pH range (1-14) and each ampoule contains the equivalent of 50mg iron per ml. Pharmacological tests have shown that the complex has a low toxicity with a LD50 (intravenous) of 400mg iron per kg in white mice.

Pharmacokinetics

After an infusion of 100mg iron as FERROSIG in 48ml 0.9% sodium chloride, at a rate of 1.7ml/min, a Cmax (in serum) of 25.1mcg/ml iron was observed. The terminal half-life was 22.4 hours. The MRT 20.2 hours and the VD (distribution volume) 2.93 litres. Renal elimination is less than 1% of the total dosage.

Iron polymaltose shows a high structural homogeneity and thus steady delivery of the complexed iron to endogenous iron binding proteins. Taken up from plasma by the reticuloendothelial system (RES), the iron is split off, binds to transferrin and partially re-enters the plasma from where it reaches the bone marrow for haemoglobin synthesis.

Indications

For the prevention and treatment of iron deficiency anaemia in the following circumstances:

- When oral therapy is contraindicated
- When enteric absorption of iron is defective
- When patient non-compliance or persistent gastrointestinal intolerance makes oral therapy impractical
- Treating iron deficiency anaemia of prematurity and that occurring in geriatric patients
- Treating iron deficiency states discovered in the third trimester of pregnancy
- Anaemia resulting from excessive blood loss
- Where contact between the doctor and patient occurs at irregular intervals

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Dosage and Administration

Intramuscular Use

Technique of Injection

The technique of injection is of crucial importance. FERROSIG should never be injected into the arm or other exposed areas. The wrong method may result in pain and discolouration of the skin.

The following method of ventro-gluteal injection according to HOCHSTETTER is recommended instead of the normal method of injection in the top outer quadrant of the gluteus maximus muscle:

- The length of the needle should be at least 5-6cm. The lumen of the needle should not be too wide.
- According to HOCHSTETTER, the site of injection is determined as follows: First point A is found, corresponding to the ventral iliac spine. If the patient lies on the right side, for instance, the middle finger of the left hand is placed on point A. The index finger is extended away from the middle finger, so that it comes to lie below the iliac crest, at point B. The triangle lying between the proximal phalanges of the middle and index fingers represents the site of injection. This is disinfected in the usual way.
- Before the needle is inserted, the skin over the site of injection is pulled down, about 2cm, to give an S-shaped puncture channel. This prevents the injected solution from running back into the subcutaneous tissues and discolouring the skin.
- The needle is introduced more or less vertically to the skin surface, angled to point towards the iliac crest rather than the hip joint.
- After the injection, the needle is slowly withdrawn and pressure from a finger applied beside the puncture site. This pressure is maintained for about one minute.
- The patient should move about after the injection.

Intravenous Use

Total dose infusion of iron polymaltose complex is recommended only when the intramuscular route is impractical or unacceptable and when bone marrow shows no stored iron. It is suitable for use in hospitals only.

The total dose to be administered, calculated from the dosage table, is aseptically added to 500ml of sterile, normal saline (up to 2500mg may be given in 500ml).

Notes

- Do not inject the iron into the tube of the administration set.
- The first 50ml should be infused slowly (5-10 drops/minute) and the patient observed carefully. If this is well tolerated, the rate may be increased to 30 drops/minute (based on a drop volume of 0.067ml).
- To avoid nausea and epigastric troubles the infusion rate should not be excessive.
- The infusion should not be mixed with any other therapeutic agents. If mixed with acidic substances or other substances with a strong reducing effect toxic iron compounds may be liberated from the compound.
- Use the diluted solution within 12 hours.

Calculation of Required Dose

The figures in the accompanying dosage table have been calculated using the following formula taken from GANZONI (Wchweiz. Med. Wschr. 100, 301-619, 1970):

$$\underbrace{\text{Weight (kg)} \times (\text{normal Hb} - \text{actual Hb in g/L}) \times 0.24}_{\text{Hb-iron deficiency}} + \text{iron depot}$$

Note: factor 0.24 = 0.0034 x 0.07 x 1000 (for the purposes of this calculation iron content of the haemoglobin =

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0.34%, blood volume = 7% of the body weight, 1000 is the conversion from grams to milligrams).

The above formula can also be used to calculate the total iron deficit.

Example of Calculation
Assuming patient weighing 60kg, normal Hb 150g/L, actual Hb 60g/L then
HB-iron deficiency = 60 x (150-60) x 0.24 = 1296mg + 500mg = 1800mg iron
Therefore patient requires 1800mg iron or 18 ampoules.

The requirements of iron reserves (stored iron) (ca. 15mg per kg up to a weight of about 34kg, total of 500mg about 34kg body weight).

	Body weight <34kg	Body weight >34kg
Normal Hb	130g/L	150g/L

Dosage Table
Dosage table for the determination of the total millilitres of FERROSIG injection required.

Body weight kg	Hb 60g/L		Hb 75g/L		Hb 90g/L		Hb 105g/L	
	mL	ampoules	mL	ampoules	mL	ampoules	mL	ampoules
5	3	1.5	3	1.5	3	1.5	2	1
10	6	3	6	3	5	2.5	4	2
15	10	5	9	4.5	7	3.5	6	3
20	13	6.5	11	5.5	10	5	8	4
25	16	8	14	7	12	6	11	5.5
30	19	9.5	17	8.5	15	7.5	13	6.5
35	25	12.5	23	11.5	20	10	18	9
40	27	13.5	24	12.	22	11	19	9.5
45	30	15	26	13	23	11.5	20	10
50	32	16	28	14	24	12	21	10.5
55	34	17	30	15	26	13	22	11
60	36	18	32	16	27	13.5	23	11.5
65	38	19	33	16.5	29	14.5	24	12
70	40	20	35	17.5	30	15	25	12.5
75	42	21	37	18.5	32	16	26	13
80	45	22.5	39	19.5	33	16.5	27	13.5
85	47	23.5	41	20.5	34	17	28	14
90	49	24.5	43	21.5	36	18	29	14.5

Administer 2ml by intramuscular injection every second day until the total dose is attained or administer 4ml at longer intervals. Regular determination of Hb level is recommended.

Maximum Single Daily Dose by Intramuscular Injection
Infants up to 5kg body weight: 0.5ml
Children of 5-10kg body weight: 1ml
Patients weighing >10kg to 45kg: 2ml

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Adults: 4ml

Contraindications

FERROSIG should not be given to patients presenting with any of the following conditions:

- Hypersensitivity to iron(III) hydroxide polymaltose complex
- Anaemia not caused by simple iron deficiency (e.g. haemolytic anaemia, megablastic anaemia caused by Vitamin B_{12} deficiency, disturbances in erythropoesis, hypoplasia of the marrow)
- Iron overload (e.g. haemochromatosis, haemosiderosis)
- Ostler-Rendu-Weber syndrome
- Chronic polyarthritis
- Bronchial asthma
- Infectious renal complaints in acute phase
- Uncontrolled hyperparathyroidism
- Decompensated hepatic cirrhosis
- Infectious hepatitis
- During the first trimester of pregnancy

As elemental iron tends to accumulate in inflamed tissues parenteral iron should not be given to patients with severe inflammation or infection of the kidney or liver.

Warnings and Precautions

Parentally administered iron preparations can cause allergic or anaphylactoid reactions. In the case of a mild allergic reaction, antihistamines should be administered immediately. Facilities for cardiopulmonary resuscitation must be available. Caution is recommended in patients with allergies and hepatic and renal insufficiency. The incidence of undesirable side effects in patients with angiocardiopathy may increase the related cardiovascular complications.

Patients with bronchial asthma, with low iron binding capacity and/or folic acid deficiency are particularly at risk of an allergic or anaphylactoid reaction. Parenterally administered iron preparations can unfavourably influence the course of infections in children.

Some cases of anaphylactic reactions after parenteral administration of iron having been described, it is recommended to initiate the treatment with a test dose to test the sensitivity of the patient.

Use in pregnancy and lactation

FERROSIG should not be administered in the first trimester of pregnancy. FERROSIG should only be administered in the second and third trimester of pregnancy if the benefits of treatment outweigh the potential risk to the foetus. No controlled studies are available on animals or on pregnant women.

Adverse Effects

Adverse reactions to parenteral FERROSIG have only been reported infrequently. However, the following reactions are known to have occurred after parenteral iron therapy:

Intramuscular Injection

Local reactions may include pain at the site of injection, local inflammation with inguinal lymphadenopathy, and lower quadrant abdominal pain. Systemic reactions after this form of administration are rare but may include anaphylaxis. (Reference is made to the following paragraph describing delayed systemic reactions).

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Intravenous Drip Therapy

Systemic reactions may include headache, nausea, vomiting, joint and muscle pains, faintness, tachycardia, flushing, sweating, bronchospasm with dyspnoea, hypotension, dizziness and circulatory collapse.

Delayed systemic reactions

Delayed systemic reactions may include dizziness, syncope, a sensation of stiffening of the arms, legs or face, chest and back pain, arthralgia, chills, fever, rash, urticaria, angioneurotic oedema and generalised lymphadenopathy.

Interactions

As with all parenteral iron preparations, FERROSIG ampoules should not be administered concomitantly with oral iron preparations as the absorption of oral iron is reduced. Oral iron therapy should not commence until at least one week after the last iron injection.

Concomitant administration of ACE inhibitors can increase the systemic effect of parenteral iron preparations.

Overdosage

Not available.

Pharmaceutical Precautions

The ampoules should be stored below 25°C. Do not freeze. Protect from light. When diluted in saline the solution should be used within 12 hours.

Medicine Classification

Prescription Medicine.

Package Quantities

Cartons of 5 x 2ml ampoules, each ampoule containing 100mg Fe as iron polymaltose.

Further Information

FERROSIG contains a macromolecular spherocolloidal complex of iron(III) hydroxide and the carbohydrate ligand polymaltose. The complex has a molecular weight of about 462,000.

The aqueous colloidal solution is sterile, pyrogen-free and approximates the pH and tonicity of the tissues.

Excipients

Water - purified, sodium hydroxide (for pH adjustment).

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